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(54) Title: ACTIVE IMMUNIZATION TO GENERATE ANTIBODIES TO SOLUBLE A-BETA

(57) Abstract: The invention provides methods useful for effecting prophylaxis or treatment of Alzheimer's disease. Such methods entail administering A-beta fragments from a central or C-terminal regions of A-beta. Such fragments can induce a polyclonal mixture of antibodies that specifically bind to soluble A-beta without binding to plaques. The antibodies can inhibit formation of amyloid deposits of A-beta in the brain of a patient from soluble A $\beta$  thus preventing or treating the disease. Fragment A-beta 15-24 and subfragments of 5-10 contiguous amino acids thereof are preferred immunogens due to their capacity to generate a high titer of antibodies.

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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/02856

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/85, 15/86; A61K 39/00, 39/395; C07K 5/00

US CL : 530/300,350.387.3; 424/130.1,178.1,184.1; 435/325

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/300,350.387.3; 424/130.1,178.1,184.1; 435/325

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SOLOMON, B. Immunological Approaches as Therapy for Alzheimer's Disease. Vaccines & Antibodies December 2002, Vol.2, No. 8, pages 907-017, entire document.	1-102
A	BARD, F. ET AL. Epitope and isotype specificities of antibodies to b-amyloid peptide for protection against Alzheimer's disease-like neuropathology. PNAS 18 February 2003, Vol. 100, No.4, pages 2023-2028, entire document.	1-102
A	LEVERONE, J.F. ET AL. Ab1-15 is less immunogenic than Ab1-40/42 for intranasal immunization of wild-type mice but may be effective for "boosting". Vaccine 16 May 2003, Vol. 21, No. 17-18, pages 2197-2206, entire document.	1-102
A	HOLTMAN D.M. ET AL. Ab immunization and anti-Ab antibodies: potential therapies for the prevention and treatment of Alzheimer's disease. Advanced Drug Delivery Reviews 7 December 2002, Vol. 54, No. 12, pages 1603-1613, entire document.	1-102
A	SIGURDSSON, E.M. A safer vaccine for Alzheimer's disease? Neurobiology of Aging November/December 2002, Vol. 23, No. 6, pages 1001-1008, entire document.	1-102



Further documents are listed in the continuation of Box C.



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\* Special categories of cited documents:

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## C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/0162129 A1 (LANNEFLT, L. ET AL.) 31 October 2002 (31.10.2002), especailly paragraph 0017, 0020, 0032, 0035-0041, page 8.	1, 4-6, 8, 14, 17, 27, 28, 48, 51-53, 55, 61, 64, 74, 75, 96, 99-102
X	US 2002/0094335 A1 (CHALIFOUR, R. ET AL.) 18 July 2002 (18.07.2002), paragraph 0020-0024, 0079-0112, pages 18-20.	1, 4-6, 8, 14, 17, 27, 28, 48, 51-53, 55, 61, 64, 74, 75, 96, 99-102
X	SCHENK, D. ET AL. Immunization with amyloid-b attenuates Alzheimer-disease-like pathology in the PDAPP mouse. Nature 8 July 1999, Vol. 400, No. 6740, pages 173-177, especially Figures 1-6.	1, 4-6, 8, 48, 51-53, 55, 57-58, 96, 99-102
X	SIGURDSSON, E.M. ET AL. Immunization with a Nontoxic/Nonfibrillar Amyloid-b Homologous Peptide Reduces Alzheimer's Disease-Associated Pathology in Transgenic Mice. American Journal of Pathology August 2001, Vol. 159, No. 2, pages 439-447, especially Figure 3.	1, 4-6, 8, 48, 51-53, 55, 57-58, 96, 99-102
X	LEMERE, C.A. ET AL. Intranasal immunotherapy for the treatment of Alzheimer's disease: Escherichia coli LT and LT(R192G) as mucosal adjuvants. Neurobiology of Aging November/December 2002, Vol. 23, No. 6, pages 991-1000, especially Tables 1-2, Figures 1-3.	1, 4-6, 8, 48, 51-53, 55, 57-58, 96, 99-102

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International Application No.  
PCT/US04/02856

Continuation of B. FIELDS SEARCHED Item 3:

WEST (USPT,PGPUBS,JPO,EPO,DERWENT) MEDLINE (PUBMED) STN (BIOSCIENCE)

abeta, beta-amyloid, Alzheimers disease, vaccine, immunogenic fragment, antibody, antigen, epitope